UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/822,186	03/20/1997	DAVID C RUEGER	CRP-137	6062

7590 07/01/2003

JAMES F. HALEY
FISH & NEAVE
1251 AVENUE OF THE AMERICAS
NEW YORK, NY 100201104

EXAMINER	
ROMEO, DAVID S	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

[redacted]

Office Action Summary	Application No.	Applicant(s)	
	08/822,186	RUEGER ET AL.	
	Examin r	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on th cover sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-25,31-33,35 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-25,31-33,35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-9,11-25,31-33,35 and 36* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *46* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendment filed April 11, 2003 (Paper No. 45) has been entered. Claims 1-9, 11-25, 31-33, 35 and 36 are pending.

Applicant's election with traverse of group III in Paper No. 45 is acknowledged. The traversal is on the ground(s) that the four members of the Markush group are "sufficiently few" and the examiner must examine all of them together. This is not found persuasive because if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility. In the present case, the compounds included within the Markush group do not share a substantial structural feature disclosed as being essential to that utility. Furthermore, separate classification (i.e., class and subclass) of distinct inventions is sufficient to establish a prima facie case that the search and examination of the plural inventions imposes a serious burden upon the Examiner. See M.P.E.P. § 803. Such separate classification is set forth in the Office action

mailed January 13, 2003 (Paper No. 44). Furthermore, the multifactorial nature of Applicant's invention and the embodiments within embodiments of Applicant's invention, does not render the members of the Markush group so "sufficiently few" as the absolute number of members of the Markush group would appear to indicate.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election of the species "single osteogenic species OP-1", "single matrix species collagen, and "single cellulose species carboxymethylcellulose" in Paper No. 45 is acknowledged.

Claims 1-9, 11-16, 20-24, 32, 33, 35, 36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), to the extent that they are drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 44. Claims 6, 9, 14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species.

Claim Rejections - 35 USC § 103

Claims 1-5, 7, 8, 11-13, 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amman (a46) and Ron (AK, cited by Applicants).

Amman discloses a formulation suitable for inducing bone formation that contains about 0.5 μg to about 5 mg of transforming growth factor-β and about 140 mg to about 50 g of tricalcium phosphate and a polymer for enhancing consistency of the formulation (column 8,

lines 38-48), wherein the "polymer for enhancing consistency of the formulation" may be any polysaccharide or insoluble protein material useful for binding the TGF-β to the TCP to form a smooth, moldable putty or paste, such as carboxymethyl cellulose and collagen, or a combination of these (column 9, lines 58-68). Amman does not teach a binding agent with a degree of substitution of 0.65-0.90.

Ron discloses pharmaceutical formulations designed to sequester osteogenic proteins in-situ for a time sufficient to allow the protein to induce cartilage and/or bone formation (column 1, full paragraph 1), wherein the osteogenic proteins are those of the BMP family identified as BMP-1 through BMP-8 (column 2, lines 47-51), wherein the osteogenic protein-sequestering material is carboxymethylcellulose (CMC) with a 0.7 degree of substitution (column 6, full paragraph 2). Ron does not teach pharmaceutical formulations comprising TCP.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a formulation suitable for inducing bone formation that contains TGF-β, TCP, carboxymethyl cellulose, and collagen, as taught by Amman, and to modify this teaching by using CMC with a 0.7 degree of substitution, as taught by Ron, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order to sequester osteogenic proteins in-situ for a time sufficient to allow the protein to induce cartilage and/or bone formation.

It would have been further obvious to one of ordinary skill in the art at the time of Applicants' invention to substitute osteogenic proteins of the BMP family identified as BMP-1 through BMP-8, as taught by Ron, in the formulation, as taught by Amman, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this

modification because one of ordinary skill in the art would have a reasonable expectation that either osteogenic proteins of the BMP family identified as BMP-1 through BMP-8 or TGF-β would perform their expected functions, i.e., bone induction, and achieve their expected results, i.e., bone repair.

Claims 1, 15, 16, 32, 33, 35, 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amman (a46) and Ron (AK, cited by Applicants) as applied to claim 1 above and further in view of Arnaud (v8) and Turco (w8).

The teachings of Amman and Ron are discussed above. Amman and Ron are silent with respect saline.

Arnaud teaches that the association of TGF-β1 in fibrin and coral induced an area of the bone growth higher than in any other groups ($P < 0.05$). Two months after surgery, this triple association induced a better healing of the defect than coral alone or control group. See the Abstract. Arnaud also teaches preparation of TGF-β1 in saline for making the composite (page 493, right column, full paragraph 1).

Turco teaches that proper electrolyte concentration and balance in plasma and tissues are critical for proper body function and that the electrolytes in normal saline more closely approximate the composition of the extracellular fluid than solutions of any other single salt (page 1570, column 2, bottom).

Arnaud and Turco do not teach an osteogenic device comprising CMC. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make an osteogenic device comprising CMC, as taught by Amman and Ron, and to modify that

teaching by making a device comprising saline, as taught by Arnaud and Turco, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because preparing the osteogenic protein in saline would allow one of ordinary skill in the art to adjust the concentration of the osteogenic protein so that an appropriate amount of osteogenic protein could be added to the device and the desired concentration of osteogenic protein in the device could be achieved and because the electrolytes in normal saline more closely approximate the composition of the extracellular fluid than solutions of any other single salt.

It would have been further obvious to one of ordinary skill in the art at the time of Applicants' invention to house the osteogenic protein agent, matrix agent, binding agent, and wetting agent in separate receptacles or combinations of agents in the same receptacle with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order to vary the concentration of the agents in order to maximize effectiveness of the agents. One of ordinary skill in the art would be motivated to make this modification in order to vary the composition of the device in terms of agents so that their concentrations are adequately formulated to optimize the devices structure and the osteoinduction which needs to occur. One of ordinary skill in the art would be motivated to combine agents in single receptacle in order to provide a ready use pre mix for a particular application.

The invention is prima facie obvious over the prior art.

[redacted]

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7-9, 11-16, 20-22, 32, 33, 35, 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim is directed to or encompasses "an osteogenic protein." This is a genus claim. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, BMPs alone are insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claims 1-9, 11-16, 32, 33, 35, 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Support for the limitation "the device does not comprise a demineralized bone matrix" cannot be found in the disclosure, as originally filed, and the introduction of such a limitation raises the issue of new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-9, 11-25, 31-33, 35 and 36 are indefinite because they recite the term "naturally occurring sources." Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "naturally occurring sources" an artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claims 1-9, 11-16, 32, 33, 35, 36 are indefinite because they recite the term "synthetic polymer matrix". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "synthetic polymer

matrix" an artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claims 1-9, 11-25, 31-33, 35 and 36 are indefinite over the recitation of "viscosity of about 10-200 cP" because viscosity of cellulosic materials depends upon the concentration. The metes and bounds are not clearly set forth. See Bulletin VC-453C, page 7, full paragraph 1.

Claims 1-5, 7, 8, 15, 16, 20-24, 32, 33, 35, 36 are indefinite because they recite the term "derivatives thereof". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "derivatives thereof" an artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claims 2, 3 are indefinite because they recite the term "variants". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "variants" an artisan cannot determine what additional or material functional limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth. It is suggested that the claims be limited to conservatively substituted variants.

Claims 32, 33, 35, 36 are indefinite because it is unclear if the "kit" comprises the device of claim 1, or if "for inducing ... using the device of claim 1" is merely an intended use of the "kit." The metes and bounds are not clearly set forth. It is suggested that the claims recite a "kit comprising the device of claim 1."

Claim Objections

Claims 20, 22-24 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The terms "fewer parts" and "fewer than" encompass zero parts. Zero parts fails to further limit and does not infringe a part.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306
AFTER FINAL (703) 872-9307

IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
JUNE 29, 2003

[redacted]